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Prevalence of masked and nocturnal hypertension in patients with obstructive sleep apnea syndrome

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ABSTRACT

Introduction: Obstructive sleep apnea (OSA) is considered as a risk factor for the development and worsening of compensation of arterial hypertension and other cardiovascular diseases. Prevalence of masked and nocturnal hypertension can have a significant negative impact on these patients and these prevalences are not well known.

Aim: To evaluate the prevalence of masked and nocturnal hypertension in patients with OSA.

Materials and methods: In this study, 97 (88 men) patients were enrolled, average age 53.9 ± 9.7 years. OSA was diagnosed with polysomnography and the continuous positive airway pressure therapy has been indicated according to current guidelines. Then were evaluated parameters of OSA (apnea-hypopnea index (AHI), oxygen desaturation index (ODI), % of sleep time <90% SpO_2, average night SpO_2). Patients also underwent physical examination including office blood pressure measurement, 24 h blood pressure monitoring (ABPM) and measurement of anthropometric parameters.

Results: Following average values were present in OSA patients (mean value and standard deviation): AHI 54.6 ± 22.7, ODI 58.3 ± 24, % of sleep time < 90% SpO_2 35.4 ± 25.1, average night SpO_2 88.8 ± 5. Masked hypertension was present in 55 (56.7%) patients, nocturnal hypertension in 79 (81.4%) patients. Arterial hypertension was appropriately compensated in only 15 (15.5%) patients. Results have not shown any statistically significant correlation between prevalence of nocturnal hypertension and AHI ($p = 0.059$), % of sleep time <90% SpO_2 ($p = 0.516$), average night SpO_2 ($p = 0.167$). ODI was significantly higher in patients with nocturnal hypertension ($p = 0.002$). No correlation between prevalence of masked hypertension and AHI ($p = 0.841$), ODI ($p = 0.137$), average night SpO_2 ($p = 0.991$) and % of sleep time <90% SpO_2 ($p = 0.896$) has been present.

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Abbreviations: ABPM, 24 hour ambulatory blood pressure monitoring; AHI, apnea-hypopnea index; BMI, body mass index; D I, II, masked hypertension definition III; MH, masked hypertension; NH, nocturnal hypertension; ODI, oxygen desaturation index; OSA, obstructive sleep apnea; mBP, mean blood pressure; SpO_2, blood oxygen saturation; BP, blood pressure.

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Conclusion: This study has demonstrated high prevalence of masked and nocturnal hypertension in patients with OSA, which can considerably increase risks of cardiovascular diseases in these patients.

Introduction

Obstructive sleep apnea (OSA) is a common chronic disorder and its clinical presentation has been well known for many centuries. In 330 AD Claudius Aelianusensus described typical signs of OSA in the king of Portus, whose servants had to awake him with needles to avoid choking. Prevalence of this disorder is described in 2–4% of middle aged individuals [1]. Common signs are snoring with apneic and hypopneic pauses and frequent micro arousals [2]. Consequences are disturbance of sleep architecture and repeated awakening, which can be accompanied by insomnia, nocturnal polyuria and dry mouth. Patients suffer from poor quality of sleep and pronounced tiredness. Increased sleepiness occurs during daytime and mainly while performing monotone activities. Concentration and memory are worsening, depression and sexual dysfunctions could also occur [3].

Nowadays, this syndrome is considered as a risk factor for development of cardiovascular and metabolic disorders such as ischemic heart disease, arterial hypertension, diabetes mellitus, heart conductance abnormalities and cerebrovascular disorders [4–6]. Nevertheless, only a limited number of physicians are evaluating sleep disorders – in our pilot study only 13% of all physicians treating patients with heart arrhythmias were directly asking patients about this syndrome. Same situation can be expected in other groups of high risk patients [6].

Relationship between OSA and arterial hypertension is under intensive evaluation because arterial hypertension doubles the risk of cardiovascular diseases (including myocardial infarction), congestive heart failure, ischemic and hemorrhagic stroke, renal failure and diseases of peripheral arteries [7].

Arterial hypertension is present in approximately 50% of patients with OSA. In comparison, the common prevalence of arterial hypertension in population of same patients without OSA is 30% [8]. OSA is increasing the risk of arterial hypertension independently on other factors – Sleep Heart Health Study showed linear correlation between systolic and diastolic blood pressure level and severity of OSA [9]. In these patients, arterial hypertension is present mostly during night and it has a form of so called non-dipper type (blood pressure level during nighttime is the same or higher than during the day) [5,10]. In patients with resistant arterial hypertension, OSA is present in up to 83% of patients [11]. From these findings emerges the fact that in all patients with resistant arterial hypertension (patients taking combination of at least three antihypertensive drugs, one of which is a diuretic) OSA should be excluded.

Masked hypertension (MH) is defined as a blood pressure which is higher during home measurement-24 h blood pressure monitoring (ABPM) or self monitoring) than casual blood pressure level measured in an office [12]. Prevalence of masked hypertension in general population is estimated to be 10–25% [13–15]. An arbitrary threshold of masked hypertension was defined as blood pressure >135/85 mmHg measured by ABPM during daytime [13]. Mere assessment of blood level pressure during the day does not detect nocturnal hypertension which then remains unrecognized. The prevalence of cardiovascular complications in patients with MH is twice as high as in common population and MH is significantly under diagnosed [16]. In previous years, only few studies have evaluated the prevalence of MH in patients with OSA [17,18]. Common finding of these studies is the fact that prevalence of MH is higher in OSA patients in comparison with general population.

The aim of this study was to assess the prevalence of masked and nocturnal hypertension in patients with OSA indicated for continuous positive airway pressure therapy according to current guidelines and to evaluate their dependency on parameters of OSA.

Materials and methods

97 patients (88 male) were enrolled in this study, average age 53.9 ± 9.7 years. We included consecutively examined patients from Sleep laboratory of Department of Respiratory Medicine, Palacky University and University Hospital Olomouc with diagnosis of OSA (using polysomnography (Alice 5, Respironics, USA)) who were indicated for continuous positive airway pressure therapy (CPAP) (apnea-hypopnea index >15). Out of included patients, 84 had a history of previously treated arterial hypertension and they were treated with substances from all of main pharmacotherapeutical classes of antihypertensive drugs. Then we evaluated parameters of OSA: apnea-hypopnea index (AHI), oxygen desaturation index (ODI), average night SpO_2 a % of sleep time <90% SpO_2. Than we performed physical examination including blood pressure (BP) measurement (standard sphygmomanometer, average of second and third measurement as a result), according to guidelines arterial hypertension threshold was defined as 140/90 mmHg. Later we measured following parameters: body mass index (BMI-patient's weight (kg)/height $(m)^2$), waist and hip circumference and Epworth sleepiness scale.

Following exclusion criteria were applied in this study: ejection fraction <50%, significant heart valve disorder, diagnosed cause of secondary arterial hypertension other than OSA, pulmonary fibrosis, chronic obstructive pulmonary

disease stage III and IV according to GOLD 2011 classification, patients with central sleep apnea, patients with low compliance and patients taking medication that could interfere with parameters followed in this study.

We also performed ambulatory blood pressure monitoring (ABPM) using Spacelabs (Spacelabs Healthcare) device. Following arbitrary values were defined as targets: mean measured blood pressure (mBP) 130/80 mmHg for 24-h interval; mBP 135/85 mmHg during daytime and mBP 120/70 mmHg during night [19]. Patient meets diagnostic criteria for masked/nocturnal hypertension when he/she presents normal office BP together with abnormal result from whichever of above mentioned BP intervals (systolic and also diastolic BP).

For requirements of this study two definitions of masked hypertension were chosen.

D I. Normal office BP together with abnormal mBP according to ABPM in whichever measured interval.

D II. Normal office BP together with abnormal mBP according to ABPM measured during daytime.

Two definitions of masked hypertension were chosen to help us evaluate changes in prevalence of MH when taking nocturnal hypertension into account.

Nocturnal hypertension (NH) was defined as mBP during night >120/70 mmHg irrespective of blood pressure level measured in office.

White coat syndrome was defined as an abnormal office BP together with normal mBP measured by ABPM.

Correct BP compensation was defined as an office BP <140/90 mmHg and all mBP measured by ABPM in normal range.

This study obtained all necessary institutionary review board approvals with conduction of this research.

Data were analyzed using SPSS version 15 (SPSS Inc., Chicago, USA). The normality of data was tested using the Shapiro–Wilk test. Statistical evaluation was carried out using Student's t test and the Mann–Whitney U test at significance level of 0.05.

Results

Basic clinical parameters are shown in Table 1.

Average office blood pressure and ambulatory blood pressure monitoring results are shown in Table 2.

Table 1 – Basic clinical parameters.

Basic clinical parameters	Sample ($n = 97$) ø ± SD
Male	85
Female	12
Age	53.9 ± 9.8
Apnea-hypopnea index	54.6 ± 22.8
Oxygen desaturation index	58.3 ± 24
Average night SpO_2 (%)	88.8 ± 5
% of sleep <90% SpO_2	35.4 ± 25.1
Epworth sleepiness scale	10.3 ± 5.1
Body mass index	37.9 ± 19.2

Table 2 – Average office and ambulatory blood pressure levels.

BP ($n = 97$) ø ± SD			
Office BP (mmHg)		Systolic BP	135.4 ± 13.5
		Diastolic BP	82.4 ± 10.7
ABPM mBP (mmHg)	24 h	Systolic BP	136.4 ± 13.3
		Diastolic BP	80.3 ± 8.6
	Day	Systolic BP	139.7 ± 13.5
		Diastolic BP	83.3 ± 9.2
	Night	Systolic BP	131.9 ± 15.4
		Diastolic BP	75.8 ± 9.7

Table 3 shows number and percentage of patients with correct blood pressure compensation (office blood pressure (<140/90 mmHg) or ABPM (mBP <130/80 mmHg during 24 h; <135/85 mmHg during daytime and <120/70 mmHg during night)) together with prevalence of masked hypertension (according to definition I, II), nocturnal hypertension (mBP >120/70 mmHg) and white coat syndrome.

Correct BP compensation measured by ABPM was present in only 15 (15.5%) of patients.

MH-definition I was present in 55 patients (56.7%) from the whole sample (97 patients), which represents 82.1% of patients with correct office BP level (67 patients). MH-definition II was present in 41 (42.3%) of patients from the whole sample (97 patients), which represents 61.2% of patients with normal office BP level (67 patients). Nocturnal hypertension was present in 79 (81.4%) of the whole sample (97 patients).

Prevalence of MH and NH was correlated with parameters of OSA. Student's t-test did not show significant correlation between prevalence of nocturnal hypertension and AHI ($p = 0.059$), % of sleep <90% SpO_2 ($p = 0.516$), average night SpO_2 ($p = 0.167$). ODI was significantly higher in patients with nocturnal hypertension in comparison with patients without this entity ($p = 0.002$).

Student's two-sample t-test did not show correlation between prevalence of masked hypertension and AHI ($p = 0.841$) and ODI ($p = 0.137$) and using Mann Whitney U test we did not found correlation between prevalence of MH and average night SpO_2 ($p = 0.991$) and % of sleep <90% SpO_2 ($p = 0.896$).

Table 3 – Correct BP compensation and prevalence of masked/nocturnal hypertension ($n = 97$).

	N	%
Office BP compensation	67	69.1
24 hour systolic + diastolic BP compensation	26	26.8
24 hour systolic BP compensation	30	30.9
24 hour diastolic BP compensation	46	47.4
Daytime systolic + diastolic BP compensation	33	34.0
Daytime systolic BP compensation	35	36.1
Daytime diastolic BP compensation	56	57.7
Night systolic + diastolic BP compensation	18	18.5
Night systolic BP compensation	23	23.7
Night diastolic BP compensation	31	32.0
BP compensation according to ABPM	15	15.5
Masked hypertension-D I	55	56.7
Masked hypertension-D II	41	42.3
Nocturnal hypertension	79	81.4
White coat syndrome	3	3.1

Discussion

Only a limited number of studies of prevalence of MH in patients with OSA exist. The probable reason is that if a patient presents normal office BP, hardly any physician performs ABPM. This is the case even if masked hypertension is increasing patient's cardiovascular risk [16]. Recent ERS/ESH guidelines for management of patients with obstructive sleep apnea and hypertension [20] do not mention prevalence of MH in OSA patients, and only recommend usage of ABPM or home monitoring devices for more accurate diagnostic of MH or NH.

For purpose of our study, we have intentionally chosen patients with moderate to severe OSA with indication for CPAP treatment. Probably because of this selection has our study found very high prevalence of masked hypertension in patients with OSA. MH was initially present in 55 (56.7%) of patients (when we used more strict criteria which included nocturnal hypertension) and in 42% of patients (when we uses criteria which took into consideration only mBP during daytime). In studies published by Drager et al. [17,21] and Baquet et al. [18] (who were evaluating prevalence of masked hypertension according to less strict definition), was prevalence of MH 39% and 30%. In the first case this prevalence was the same as in our study, in two other studies the prevalence of MH was slightly lower. This could be attributed to the selection of patients, e.g. Drager et al. [21] included only patients without antihypertensive treatment. When we compare our results with available literature, we can hypothesize, that in patients with more severe OSA, MH and NH are more prevalent. Based on these results, more large scale studies including subjects from whole spectrum of patients with OSA and arterial hypertension are needed.

In our study we used common criteria and also more strict criteria (D I) for MH. This is well justified in patients with OSA because of the high prevalence of nocturnal hypertension in these patients.

In the available literature we have not found any studies correlating the prevalence of MH with parameters of OSA.

Prevalence of nocturnal hypertension was very high in these patients – 81.4%. This finding is consistent with previously published data [10]. The correlation between AHI and the prevalence of nocturnal hypertension was close to reach statistical significance. Also in patients with nocturnal hypertension was ODI significantly higher. This could present evidence for higher importance of oxygen desaturation in pathophysiology of development of nocturnal hypertension than the simple presence of apneic and hypopneic pauses [22]. For better understanding of pathophysiology of nocturnal hypertension development, more studies with sufficient sample size are needed.

The mechanism how could OSA lead to development of masked hypertension is unknown. This effect could mediated by increased tone of sympathetic nervous system [23], dysregulation of renin–angiotensin–aldosterone system [24] and by endothelial dysfunction [25]. Only a limited number of studies of how OSA influences masked/nocturnal hypertension exist and nowadays, though there is no consensus about pathophysiological mechanisms of their development. One of possible explanations is a hypothesis, that even minimal stimulus leads to a development of arterial hypertension because of autonomic nervous system dysregulation.

There is not enough evidence on how to treat these patients. Only one study of the influence of continuous positive airway pressure therapy on prevalence of masked hypertension has been published. Drager et al. described reduction of MH prevalence in patients treated with CPAP [17]. Limitations of this study are the short-term treatment of patients (only 3 months) and the small sample size- only 18 patients were enrolled in this study. There is a need to conduct more studies in the future to enlighten this problem.

Because of the significant prevalence of MH in patients with OSA, we have to consider if it would be beneficial to include ABPM into polysomnographic devices. This is supported by the fact that recent ESH guidelines [16] recommend that ABPM usage improves sensitivity of prediction of serious cardiovascular events. Using this algorithm we would be able to diagnose arterial hypertension together with OSA and thus save resources needed for future evaluation of patients and improve their comfort and compliance. Baquet et al. [18] recommended usage of ABPM to identify MH when casual systolic and diastolic pressure are above 125/83 mmHg (positive predictive value >90%). Together with CPAP therapy we could concomitantly start more effective antihypertensive treatment.

One of limitations of this study is the enrollment of patients with cardiometabolic comorbidities, such as known and treated arterial hypertension, diabetes or ischemic heart disease and obesity. However, with this approach we were able to create a sample of patients that most closely reflects composition of patients referred to the sleep laboratory. Other limitation is an absence of control group of patients with identical age, gender and BMI without sleep disordered breathing, In the future, we plan to perform more studies, which will also include control group.

Conclusion

This study has shown high prevalence of masked and nocturnal hypertension in patients with OSA indicated for CPAP treatment. Unrecognized hypertension (even during daytime or night) increases the patient's risk of cardiovascular diseases. Because of these facts it is necessary to perform ABPM in all patients with OSA. Only with this approach we would be able to recognize arterial hypertension which could worsen prognosis of these patients.

Conflict of interest

No conflict of interest.

Funding body

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Ethical statement

Preparation of the manuscript has been done according to all applicable ethical standards.

Informed consent

All patients included in this study agreed to participate.

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